PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 06 March 2001 (06.03.01)	
International application No. PCT/US00/17755	**Applicant's or agent's file reference** 15280-3981PC
International filing date (day/month/year) 24 June 2000 (24.06.00)	**Priority date** (day/month/year) 09 July 1999 (09.07.99)
Applicant BUCHHOLZ, Ursula et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

19 January 2001 (19.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

ATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
15280-398-1PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/17755	24/06/2000	09/07/1999
International Patent Classification (IPC) or national classification and IPC C12N15/86		
Applicant THE GOVERNMENT OF THE UNITED STATES OF ... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19/01/2001	02.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Wimmer, G Telephone No. +49 89 2399 7347

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/17755

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-107 as originally filed

Claims, No.:

1-101 as originally filed

Drawings, sheets:

1/18-18/18 as originally filed

Sequence listing part of the description, pages:

1-7 (SEQ ID NOs. 1-23), as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 87 (entirely), 35, 48-56 (partially).

because:

   ☒ the said international application, or the said claims Nos. 48-56 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 87 (entirely), 35 (partially).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	12-15, 23, 24, 28, 29,70-72, 78, 100, 101
	No:	Claims	1-11, 16-22, 25-27, 30-34, 36-69, 73-77, 79-99
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-86, 88-101
Industrial applicability (IA)	Yes:	Claims	1-47, 57-101
	No:	Claims	

2. Citations and explanations
see separate sheet

R Item III

Non-establishment of opinion.

1) As detailed in the International Search Report, a search has been carried out for all claims except claims 87 (entirely) and 35 (partially). Consequently, the present examination was also limited to claims 1-86 and 88-101, insofar as an International Search Report had been established for subject-matter of these claims.

2) Claims 48-56 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV

Lack of unity of invention.

As detailed in the International Search Report, unity of invention was found to be lacking with the present application.
Specifically, the application was found to relate to two different inventions:

1) An isolated infectious chimeric human-bovine respiratory syncytial virus (RSV), characterized by combining a partial or complete human RSV background genome or antigenome with one or more heterologous gene(s) and/or genome segment(s) of a bovine RSV to form a human-bovine chimeric RSV genome or antigenome; and

2) An isolated infectious chimeric bovine-human respiratory syncytial virus (RSV), characterized by combining a partial or complete bovine RSV background genome or antigenome with one or more heterologous gene(s) and/or genome segment(s) of a human RSV to form a bovine-human chimeric RSV genome or antigenome.

These two groups are not so linked as to form a single general inventive concept (Rule 13.1 PCT) in the light of the prior art.

However, since the examination of both inventions does not require an undue effort, no Invitation to Restrict or to Pay Additional Fees is extended at the moment.

Re Item V

Reasoned statement under Art. 35(2) PCT with regard to novelty, inventive step or industrial applicability.

1) Reference is made to the following documents (the document numbering corresponds to their order of citation in the international search report):

D1: BUCHHOLZ, U.J. ET AL.: 'Generation of Bovine Respiratory Syncytial Virus (BRSV) from cDNA: BRSV is not essential for virus replication in tissue culture , and the human RSV Leader region acts as a functional BRSV genome promoter' JOURNAL OF VIROLOGY., vol. 73, no. 1, January 1999 (1999-01), pages 251-259, XP002154541 ICAN SOCIETY FOR MICROBIOLOGY US cited in the application

D2: WO 98 02530 A (WHITEHEAD STEPHEN S ;US HEALTH (US); COLLINS PETER L (US); JUHASZ) 22 January 1998 (1998-01-22) cited in the application

D4: WO 97 12032 A (US HEALTH ;COLLINS PETER L (US)) 3 April 1997 (1997-04-03)

The following applies to subject-matter of both Inventions I and II as defined under sect. IV.

Novelty under Art. 33(2) PCT.

2) Chimeric RSV genomes are extensively described in documents D1, D2 and D4. In particular, hybrids of bovine and human RSV are described in both documents; D2 and D4 moreover describe the creation of such hybrid viruses for the purpose of creating novel attenuated RSV for the use in vaccine preparations.

For instance, D2 specifically describes the creation of such hybrid RSV genomes through replacing the NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2) or L genes, or non-immunogenic parts of the G or F genes, with their bovine counterpart. Also, D2 describes the creation of hybrid virus through inserting attenuating sequences of human RSV into a bovine RSV backbone; it is further envisioned that a bovine- human RSV incorporates a substitution of the human RSV NP gene or gene segment with a counterpart bovine NP gene or gene segment, with optional deletions of or within the SH, NP, NS1, NS2 or other gene. Certain embodiments describe the favourable modification of such substituted genes or gene segments, by adopting point mutations from e.h. human RSV strains cpts248/404 cpts530/1009, or cpts530/1030. Finally, D2 also describes the introduction of sequences from Parainfluenza Virus (PIV) into such a recombinant RSV genome, ens further specific embodiments of the current application.

Thereby, document D2 discloses subject-matter of claims 1-11, 16-22, 25-27, 30-34, 36-42, 43-69, 73-77 and 79-99, and these claims are therefore not novel.

Inventive Step under Art. 33(3) PCT.

3) For the remaining claims (12-15, 23, 28, 70-72, 78, 100, 101) which were subject to this examination, novelty can be formally acknowledged. However, it appears that the additional features of these claims which were not disclosed in D2, merely represent modifications which do not go beyond measures routinely envisioned by the person skilled in the art, are only hypothetical modifications without support in the description by examples or do not appear to lead to a technical effect, which is surprising in the light of the prior art.
Consequently, no inventive step is acknowledged for claims 1-86 and 88-101, insofar as an International Search Report had been established for subject-matter of these claims.

Industrial Applicability under Art. 33(4) PCT.

4) For the assessment of the present claims 48-56 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

BWP

PATENT COOPERATION TREATY

NIH-0114 (Copy Sent to Client)

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KING, Jeffrey J. et al.
TOWNSEND AND TOWNSEND AND CREW LLP
Two Embarcadero Center
8th Floor
San Francisco, CA 94111-3834
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	02.11.2001
Applicant's or agent's file reference: 15280-398-1PC	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/17755 ✓	24/06/2000	09/07/1999 ✓

Applicant: THE GOVERNMENT OF THE UNITED STATES OF ... et al. ✓

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER** 11/9/02

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Faux, K Tel.+49 89 2399-8062

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
15280-398-1PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/17755	24/06/2000	09/07/1999
International Patent Classification (IPC) or national classification and IPC C12N15/86		
Applicant THE GOVERNMENT OF THE UNITED STATES OF ... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19/01/2001	02.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Wimmer, G Telephone No. +49 89 2399 7347

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/17755

I. Basis of th r p rt

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-107 as originally filed

Claims, No.:

1-101 as originally filed

Drawings, sheets:

1/18-18/18 as originally filed

Sequence listing part of the description, pages:

1-7 (SEQ ID NOs. 1-23), as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 87 (entirely), 35, 48-56 (partially).

because:

☒ the said international application, or the said claims Nos. 48-56 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 87 (entirely), 35 (partially).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity f inv nti n

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	12-15, 23, 24, 28, 29,70-72, 78, 100, 101
	No:	Claims	1-11, 16-22, 25-27, 30-34, 36-69, 73-77, 79-99
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-86, 88-101
Industrial applicability (IA)	Yes:	Claims	1-47, 57-101
	No:	Claims	

2. Citations and explanations
see separate sheet

Re Item III

Non-establishment of opinion.

1) As detailed in the International Search Report, a search has been carried out for all claims except claims 87 (entirely) and 35 (partially). Consequently, the present examination was also limited to claims 1-86 and 88-101, insofar as an International Search Report had been established for subject-matter of these claims.

2) Claims 48-56 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV

Lack of unity of invention.

As detailed in the International Search Report, unity of invention was found to be lacking with the present application.
Specifically, the application was found to relate to two different inventions:

1) An isolated infectious chimeric human-bovine respiratory syncytial virus (RSV), characterized by combining a partial or complete human RSV background genome or antigenome with one or more heterologous gene(s) and/or genome segment(s) of a bovine RSV to form a human-bovine chimeric RSV genome or antigenome; and

2) An isolated infectious chimeric bovine-human respiratory syncytial virus (RSV), characterized by combining a partial or complete bovine RSV background genome or antigenome with one or more heterologous gene(s) and/or genome segment(s) of a human RSV to form a bovine-human chimeric RSV genome or antigenome.

These two groups are not so linked as to form a single general inventive concept (Rule 13.1 PCT) in the light of the prior art.

However, since the examination of both inventions does not require an undue effort, no Invitation to Restrict or to Pay Additional Fees is extended at the moment.

Re Item V

Reasoned statement under Art. 35(2) PCT with regard to novelty, inventive st p or industrial applicability.

1) Reference is made to the following documents (the document numbering corresponds to their order of citation in the international search report):

D1: BUCHHOLZ, U.J. ET AL.: 'Generation of Bovine Respiratory Syncytial Virus (BRSV) from cDNA: BRSV is not essential for virus replication in tissue culture , and the human RSV Leader region acts as a functional BRSV genome promoter' JOURNAL OF VIROLOGY., vol. 73, no. 1, January 1999 (1999-01), pages 251-259, XP002154541 ICAN SOCIETY FOR MICROBIOLOGY US cited in the application

D2: WO 98 02530 A (WHITEHEAD STEPHEN S ;US HEALTH (US); COLLINS PETER L (US); JUHASZ) 22 January 1998 (1998-01-22) cited in the application

D4: WO 97 12032 A (US HEALTH ;COLLINS PETER L (US)) 3 April 1997 (1997-04-03)

The following applies to subject-matter of both Inventions I and II as defined under sect. IV.

Novelty under Art. 33(2) PCT.

2) Chimeric RSV genomes are extensively described in documents D1, D2 and D4. In particular, hybrids of bovine and human RSV are described in both documents; D2 and D4 moreover describe the creation of such hybrid viruses for the purpose of creating novel attenuated RSV for the use in vaccine preparations.

For instance, D2 specifically describes the creation of such hybrid RSV genomes through replacing the NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2) or L genes, or non-immunogenic parts of the G or F genes, with their bovine counterpart. Also, D2 describes the creation of hybrid virus through inserting attenuating sequences of human RSV into a bovine RSV backbone; it is further envisioned that a bovine- human RSV incorporates a substitution of the human RSV NP gene or gene segment with a counterpart bovine NP gene or gene segment, with optional deletions of or within the SH, NP, NS1, NS2 or other gene. Certain embodiments describe the favourable modification of such substituted genes or gene segments, by adopting point mutations from e.h. human RSV strains cpts248/404 cpts530/1009, or cpts530/1030. Finally, D2 also describes the introduction of sequences from Parainfluenza Virus (PIV) into such a recombinant RSV genome, ens further specific embodiments of the current application.

Thereby, document D2 discloses subject-matter of claims 1-11, 16-22, 25-27, 30-34, 36-42, 43-69, 73-77 and 79-99, and these claims are therefore not novel.

Inventive Step under Art. 33(3) PCT.

3) For the remaining claims (12-15, 23, 28, 70-72, 78, 100, 101) which were subject to this examination, novelty can be formally acknowledged. However, it appears that the additional features of these claims which were not disclosed in D2, merely represent modifications which do not go beyond measures routinely envisioned by the person skilled in the art, are only hypothetical modifications without support in the description by examples or do not appear to lead to a technical effect, which is surprising in the light of the prior art.
Consequently, no inventive step is acknowledged for claims 1-86 and 88-101, insofar as an International Search Report had been established for subject-matter of these claims.

Industrial Applicability under Art. 33(4) PCT.

4) For the assessment of the present claims 48-56 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

ATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
TOWNSEND AND TOWNSEND AND CREW LLP
Attn. KING, Jeffrey
Two Embarcadero Center
Eighth Floor
San Francisco, CA 94111-3834
UNITED STATES OF AMERICA

	Date of mailing *(day/month/year)* 03/04/2001
Applicant's or agent's file reference 15280-3981PC	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 00/ 17755	International filing date *(day/month/year)* 24/06/2000 6/23/00 per CPI
Applicant THE GOVERNMENT OF THE UNITED STATES OF AMERICA;	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

   Filing of amendments and statement under Article 19: 6/3/01
   The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

   When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

   Where? Directly to the International Bureau of WIPO
   34, chemin des Colombettes
   1211 Geneva 20, Switzerland
   Fascimile No.: (41-22) 740.14.35

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

   Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   Ch: 2 2/9/01 undocketed

   Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

   2/9/01 undocketed 6/9/02

   Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Carla Louro

Form PCT/ISA/220 (July 1998)

Amendment 6/3/01
DOCKETED km

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

ATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
15280-3981PC		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 17755	24/06/2000	09/07/1999
Applicant		
THE GOVERNMENT OF THE UNITED STATES OF AMERICA;		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [X] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   HUMAN-BOVINE CHIMERIC RESPIRATORY SYNCYTIAL VIRUS VACCINES

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] None of the figures.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/17755

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 48 to 56 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

2. [X] Claims Nos.: 87 35
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 10-15, 68-72, 92, 94-97 and partially 1-9, 30-67, 82-91, 93, 98-101

An isolated infectious chimeric human-bovine respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a RNA polymerase elongation factor, characterised by combining a partial or complete human RSV (HRSV) background genome or antigenome with one or more heterologous gene(s) and/or genome segment(s) of a bovine RSV (BRSV) to form a human-bovine chimeric RSV genome or antigenome; a method for stimulating the immune system of an individual to induce protection against RSV which comprises administering to the individual an immunologically sufficient amount of said chimeric RSV combined with a physiologically acceptable carrier; an immunogenic composition to elicit an immune response against RSV comprising an immunologically sufficient amount of said chimeric RSV combined with a physiologically acceptable carrier; an isolated polynucleotide molecule comprising said chimeric RSV genome or antigenome;

2. Claims: 16-29, 73-81 and partially 1-9, 30-67, 82-91, 93, 98-101

An isolated infectious chimeric bovine-human respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a RNA polymerase elongation factor, characterised by combining a partial or complete bovine RSV (BRSV) background genome or antigenome with one or more heterologous gene(s) and/or genome segment(s) of a human RSV (HRSV) to form a human-bovine chimeric RSV genome or antigenome a method for stimulating the immune system of an individual to induce protection against RSV which comprises administering to the individual an immunologically sufficient amount of said chimeric RSV combined with a physiologically acceptable carrier; an immunogenic composition to elicit an immune response against RSV comprising an immunologically sufficient amount of said chimeric RSV combined with a physiologically acceptable carrier; an isolated polynucleotide molecule comprising said chimeric RSV genome or antigenome;

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 87 35

Present claim 87 is related to a the "polynucleotide of claim 59". However, present claim 59 is not concerning a polynucleotide. The reference could be to claim 63, but it is not obvious and for a clarification from the applicant would be necessary.

Present claim 35 relates to a product defined by reference to a desirable characteristic namely comprising a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host range restriction or a change in immunogenicity.
The claim covers all products having this characteristic, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such productss. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products examplified in claims 30-34, 36-41, 43-45.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTER TIONAL SEARCH REPORT

In tional Application No
P S 00/17755

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/86 C12N7/04 C07K14/14 C12N15/62 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BUCHHOLZ, U.J. ET AL.: "Generation of Bovine Respiratory Syncytial Virus (BRSV) from cDNA: BRSV is not essential for virus replication in tissue culture , and the human RSV Leader region acts as a functional BRSV genome promoter" JOURNAL OF VIROLOGY., vol. 73, no. 1, January 1999 (1999-01), pages 251-259, XP002154541 ICAN SOCIETY FOR MICROBIOLOGY US cited in the application page 252, column 1, last paragraph -column 2, paragraph 2; figure 1	1,2,6-8, 16, 35-37, 46, 63-66, 83-86,88
Y	page 258, column 1, line 3 -column 2, last paragraph	1-14, 16-20, 25-28, 30-70, 82-101

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 March 2001	03 04 2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Chambonnet, F

4

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 02530 A (WHITEHEAD STEPHEN S ;US HEALTH (US); COLLINS PETER L (US); JUHASZ) 22 January 1998 (1998-01-22) cited in the application page 11, line 9 - line 20	1-3, 6-12, 30-70, 82-99
Y	page 36, line 10 -page 40, line 21; claims	1-14, 16-20, 25-28, 30-70, 82-101

Y	WO 99 24564 A (UNIV MARYLAND ;SAMAL SIBA K (US)) 20 May 1999 (1999-05-20) the whole document	16,35

X	WO 97 12032 A (US HEALTH ;COLLINS PETER L (US)) 3 April 1997 (1997-04-03)	1-10, 16-18, 30-70, 88,89
Y	the whole document	1-14, 30-70, 82-101

X	WO 99 15631 A (AVIRON INC) 1 April 1999 (1999-04-01)	1-3, 7-11,14, 35-37, 42, 46-48, 52-54, 57,60, 61,63, 82-86, 88-92, 96-99
Y	the whole document	1-11,14, 46-66, 82, 88-101

P,X	BUCHHOLZ UJ, GRANZOW H, SCHULDT K, WHITEHEAD SS, MURPHY BR, COLLINS PL.: "Chimeric bovine respiratory syncytial virus with glycoprotein gene substitutions from human respiratory syncytial virus (HRSV): effects on host range and evaluation as a live-attenuated HRSV vaccine." J VIROL. 2000 FEB;74(3):1187-99., XP000972255 the whole document	1-3,6, 10, 16-18, 20,21, 25,26

INTEP. \TIONAL SEARCH REPORT

Inform[redacted]n on patent family members

Ir. .ational Application No
P[redacted]IS 00/17755

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9802530 A	22-01-1998	AU 3799797 A	09-02-1998
		BR 9710363 A	11-01-2000
		CA 2257823 A	22-01-1998
		EP 0912724 A	06-05-1999
		US 5993824 A	30-11-1999
WO 9924564 A	20-05-1999	AU 1297299 A	31-05-1999
WO 9712032 A	03-04-1997	AU 727923 B	04-01-2001
		AU 7119296 A	17-04-1997
		CA 2230033 A	03-04-1997
		EP 0859831 A	26-08-1998
		JP 11512609 T	02-11-1999
WO 9915631 A	01-04-1999	AU 9585298 A	12-04-1999
		EP 1017791 A	12-07-2000